Prebiotics and Probiotics in Human Health: whither Nigeria?

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Abstract

This essay examines and explores the idea of prebiotics and probiotics as it has been applied and used in humans. It probes their underlying mechanisms of action(s), and underlines their importance in the context of exerting a number of physiologic and therapeutic properties, amongst others. Employing the methodological enquiry of archival research and conceptual analysis, this paper notes that although the relevance of prebiotics and probiotics has received much laudatory remarks, it is critical to look deeply and seriously into the claims of this emerging science as well as examine its limitations in a systematic manner before considering how it can be adopted in a developing nation like Nigeria.

Keywords Prebiotics, Probiotics, Health, Disease

Introduction & Conceptual Delimitation

Prebiotics and probiotics can be conceived as scientific strategies that utilise nutritionally or microbially modified food products in the maintenance of health. These modified food products are consciously used with a view to contributing positively to man and animal health status. In specific terms, Gibson and Roberfroid (1995) define prebiotics as selectively fermented food ingredients that allow specific changes both in the composition and/or activity of the gastrointestinal microflora thereby conferring benefit on host wellbeing and health. Prebiotics include inulin, short-chain fructo-oligosaccharides and oligofructose and are neither digestible nor absorbable by the body; thus, remaining in the colon where they stimulate the activity of endogenous microflora as well as promote bowel regularity (Afolabi et al, 2005). In addition, prebiotics elaborate stimulatory effects on specific microflora of the small bowel (Schrezenmeir and de Vrese, 2001). Probiotics, on the other hand, are live microbial food ingredients with benefits for health (Salminen et al, 1998) which act by improving the intestinal microbial balance (Fooks and Gibson, 2002). Principal amongst these are strains of lactobacillus and bifidobacterium. Foods such as yoghurts, cheese and dairy drinks are packed with probiotics, and this culinary practice has thrived in countries in Europe, Asia and the Americas (Afolabi et al, 2005).

Although the idea of prebiotics and probiotics are also used in animals such as for the purpose of enhancing growth and preventing early mortality ((Marteau and Boutron-Ruault, 2002); in humans their potential nutritional advantages consist of preventive and curative effects against diseases, including intestinal dysfunctions, inflammatory bowel disease and colon cancer; amongst others (Marteau and Boutron-Ruault ,2002). In this paper, we explore the notion of prebiotics and probiotics as it affects humans in the context of health and disease. We highlight their importance in terms of physiologic, therapeutic and nutritional properties, amongst others. Ultimately, we explore how the benefits of this science can be actively pursued and used for the good of the Nigerian populace.

The Human Gut Flora

As was pointed out in our introduction to this essay, prebiotics as well as probiotics modulate their beneficiary effects on the gut flora. Indeed, as pointed out by Marteau and Boutron-Ruault (2002), probiotics and prebiotics share a common mechanism of action at the level of the modification of the endogenous flora. Hence, we begin our discussion with a

brief description of the anatomy and physiology of the human gut flora, an approach that should provide a relevant background to the understanding of the mechanisms of action of prebiotics and probiotics.

Otherwise referred to as the microbiome or microbiota, the human gut flora consists of about 500 to 1000 bacterial species (Sears, 2005), about 90% of which are obligate anaerobes (Kayser et al, 2005). The most common of these bacteria species are Bifidobacterium, Clostridium, Bacteroides, Eubacterium, Escherichia, Enterococcus, Streptococcus and Klebsiella. These bacteria are commonly referred to as 'friendly' bacteria. As Oyetayo and Oyetayo (2005) point out, when the composition of the friendly gut bacteria declines and that of the 'unfriendly' ones dominate; health problems such as gas production, bloating, constipation and malabsorption can ensue.

The intestinal milieu ensures close interaction between the individual and its environment, with a constant exchange of energy, water, nutrients and electrolytes (Saavedra and Tschernia, 2002). In a similar vein, Sears (2005) notes that humans generally enjoy health through a productive collaboration with their colonizing flora, the majority of which reside in the colon. Indeed, it has been observed that these commensal organisms exert critical interdependent roles including metabolic activities that result in salvage of energy and absorbable nutrients, important trophic effects on intestinal epithelia and on immune structure and function, and protection of the colonised host against invasion by alien microbes (Saulnier et al, 2009)). The human gut flora is involved in the regulation of intestinal development and function (Grangette, et al, 2005) as well as bile acid metabolism and enterohepatic circulation (Saavedra and Tschernia, 2002). The importance of the normal gut flora is further underscored by findings from the Human Genome Project which support the idea that humans derived 233 proteins from their resident flora (Relman and Falkow, 2004).

Summarily, the human gut flora plays the following roles (Sears, 2005; Hooper, 2006):

- Polysaccharide utilisation and nutrient release
- Enhanced fat storage
- Induction of mucosal glucose transporters
- Induction of villous capillary formation
- Induction of selected proteins of innate immunity

- Mucosal homeostasis and repair
- Stimulation of Ig A
- Development of gut associated lymphoid tissue (GALT)
- Diversification of lymphoid populations and immunoglobulin genes

Bearing all these roles in mind, it can therefore be generally stated that probiotics and prebiotics exploit these critical functions in conferring their various health benefits.

Probiotics: General Features

The idea of probiotics can be said to have emerged in the early 1900s following the works of such men as Henry Tissier and Elie Metchnikoff (Oyetayo and Oyetayo, 2005). Tissier, a French Paediatrician, had observed that children with diarrhoea had low numbers of Y-shaped bacteria in their stools as opposed to healthy children. On the other hand Metchnikoff, the Nobel Laureate Immunologist, hypothesized that the long, healthy lives of Bulgarian peasants was due to their consumption of fermented milk. Against that background, he proposed that lactobacilli could prevent or minimise the harmful effects of The putrefactive microbes associated with gastrointestinal diseases (Furie, 2005).

Principal organisms that have been hitherto used as probiotic agents include strains of Lactobacilli such as *L. acidophilus, L. casei, L. crispatus, L. paracasei, L. plantarum L. reuteri, and L. rhamnosus*; and strains of Bifidobacteria such as *B. adolescentis, B. animalis, B. bifidum, B. breve, B. infantis, B. lactis and B. longum* (Furie, 2005). Other probiotic organisms include *B. sublitis, E. faecalis, L. lactis and Strep. thermophilis.*

Since the introduction of the first probiotic fermented food drink in Japan called Yakult in 1935 (Anukam, 2007), considerable strides have been made in the field of probiotics. And although, there is still need for more productive human trials (Hamilton-Miller, 1999), it can be safely said that the science of probiotics has come to stay.

Mechanism of Probiosis

The specific mechanisms through which probiotic agents act are determined by the nature of the given function. That is, there are multiple probiotic mechanisms (Saulnier et al, 2009). Hence our discussion of probiosis would be along the lines of the intended purpose(s).

Probiotic Protection Against Pathogens

Probiotics can enhance host defense system against an array of pathogens. Mucin production and reduction of gut permeability is one such means through which this can occur, and these prevent the penetration of pathogenic organisms and toxic substances (Saulnier et al, 2009). Other substances that are antibiotic in nature can likewise be produced by probiotic agents. These include organic acids (e.g. lactate and acetate), peptides and proteins (e.g. reuterin, lantibiotics, bacteriocin, bacteriolysin that exert inhibitory effects on pathogens (Cheikhyoussef et al, 2008; Saulnier et al, 2009) as well as diacetyl and H_2O_2, hydrogen peroxide (Parracho, McCartney and Gibson, 2007).

Probiotic Inhibition of Attachment and Nutrient Deprivation

Probiotic organisms may also act by adhering to the mucosal surface, thereby resisting peristalsis and preventing other species from adhering. In fact, the ability to compete for limited nutrients is an important factor that determines the composition of the gut flora. Hence, increasing the probiotic concentration decreases the substrate available for other species (Fooks and Gibson, 2002).

Probiotic Immunomodulation

Galdeano et al (2007) have proposed that probiotics can stimulate or suppress different aspects of the immune system. The immunostimulatory activity occurs through boosting pro-inflammatory cytokine expression, increasing mucosal antibody production and enhancing host defensin production (Saulnier et al, 2009); while immunosuppressive activity can be elaborated via decreasing cytokine expression, systemic inflammation, cellular proliferation and promoting apoptosis (Saulnier et al, 2009). Other mechanisms include enhanced substrate uptake as well as degradation of toxin receptors (Fooks and Gibson, 2002). We will now examine the use of probiotic agents in specific instances.

Lactose Intolerance

Lactose intolerance is common throughout the world, and is related to the deficiency of the enzyme β-galactosidase in the intestinal mucosa (Parracho, McCartney and Gibson, 2007). Lactose is therefore undigested, an event that clinically manifests as abdominal distension, flatulence and watery diarrhoea. Probiotic bacteria such as lactobacilli and bifidobacteria have been used in the alleviation of this condition. These probiotic agents act

by increasing the endogenous production of β-galactosidase which then improves lactose digestibility in the small intestine (Rastall et al, 2000; Parracho, McCartney and Gibson, 2007), thus alleviating the unpleasant symptoms.

Constipation

Constipation is a condition characterised by slow gastrointestinal transit time which leads to infrequent bowel movement, thus producing small hard faeces or difficult painful defecation, in addition to discomfort, distension and abdominal bloating (Salminien et al, 1998; Parracho, McCartney and Gibson, 2007). Probiotics have been explored and used to modulate the metabolic activity of the colonic microflora in order to improve intestinal motility and reduce faecal enzyme activity ((Parracho, McCartney and Gibson, 2007).

Atopic Diseases

Probiotics have been found to be of use in the prevention and management of atopic diseases such as eczemas ((Parracho, McCartney and Gibson, 2007). In this context, *Lactobacillus rhamnosus* GG (LGG) and other lactobacilli are found to hydrolyse purified casein into smaller peptides and amino acids and thus decrease the proliferation of mitogen-induced lymphocytes compared to non-treated caseins (Sutas et al, 1996). The effects of LGG in the prevention of atopic diseases have also been studied in pregnant women from atopic-prone families (Nova et al, 2007). Rautava, Kalliomaki and Isolauri (2002) explained this effect via the increased levels of anti-inflammatory transforming growth factor β_2 (TGFβ_2) that was found in the probiotic group compared to those women who received placebo.

Allergies

Furie (2005) remarks that a number of probiotic agents have been used in allergic conditions. These include LGG (for rhinitis, eczema, food allergies and asthma), *B. lactis (*for atopic eczema), *L. paracasei* (for allergic rhinitis) and *L. reuteri* (for atopic dermatitis). These agents are thought to mediate their action via the induction of cytokine production which ultimately regulate the activities of blood cells such as leukocytes and null K cells (Nova et al, 2007).

Cancer

Probiotics have been used in the palliation and/or remission of such malignant conditions as colon cancer and breast cancer. Their mode of action in these conditions have been explained by parameters such as induction of cytokines including interleukine-6 and tumour necrosis factor-α as well as increased synthesis of inducible nitric oxide synthase enzyme (de Moreno de LeBlanc, Matar and Perdigon, 2007). Despite the very encouraging results obtained from the anticancer use of probiotics, there are still some big gaps in our knowledge especially as regards the precise mechanism involved (Rowland, 2004).

Some of the other areas where probiotics have been used include management of psychological and physical stress, a miscellany of infectious conditions, eating disorders especially, anorexia nervosa (Nova et al, 2007) as well as blood lipid lowering (Hamilton-Miller, 1999), gastritis due to *H. Pylori* (Fooks and Gibson,. 2002), regulation of glucose metabolism (Laitinen, Poussa and Isolauri, 2008), acute otitis media and aging (Rautava, Salminien and Isolauri, 2008).

Quality Assurance Considerations

The presence of potentially pathogenic species such as *Enterococcus faecium and E. faecalis* in probiotics demands that the production and marketing of probiotic-containing products be carefully monitored and controlled (Brink, Senekal and Dicks, 2005).Indeed, certain criteria and measures have been instituted to ensure that probiotics actually confer their health claims to consumers. That is, there are a number of characteristics required of a good prebiotic agent. According to Fuller (1989), the following features are expected of good probiotic strain:

- Clear evidence of benefits to health
- Non-pathogenicity as well as non-toxicity
- Ability to survive and be metabolised in the gut
- Stability and viability under storage and field conditions

Taking these factors into consideration, probiotics can be produced in the form of capsules, paste, powder or granules (Oyetayo and Oyetayo, 2005).

Prebiotics: General Characteristics

Prebiotics, as mentioned earlier, are non-digestible food ingredients that exert their activities through " selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon" (Gibson and Roberfroid, 1995). Certain oligosaccharides that can not be digested except be bacterial action are considered as prebiotics (Fooks and Gibson, 2002). However, there exists a general criteria for determining what and what does not constitute prebiotic. As advanced by Gibson and Roberfroid (1995), these are:

- It must be neither hydrolysed nor absorbed in the upper part of the gastrointestinal tract.
- It must undergo selective fermentation by one or a limited number of the potentially beneficial bacteria kin the colon.
- Alteration of the composition of the colonic microbiota towards a healthier composition.
- Induction of effects that are beneficial to the host's health.

Non-digestible oligosaccharides, fructo-oligosaccharides, gluco-oligosaccharides, galacto-oligosaccharides, isomalto-oligosaccharides, soybean-oligosaccharides and transgalacto-oligosaccharides are all considered as prebiotics (Hayakawa et al, 1990; Gibson and Roberfroid, 1995). Having said this much, let us now explicate the mechanism (s) of prebiosis that have been established.

Mechanism of Prebiosis

The effects of prebiotics have been generally directed towards the colon (Saulnier et al, 2009). However, some evidence is emerging showing that prebiotics can indeed exert their effects beyond the gastrointestinal tract (Lenoir-Wijnkoop et al, 2007). Because prebiotics exploit the use of non-viable dietary components to improve gut health, the range of foods to which they can be added is much wider than for probiotics (Parracho, McCartney and Gibson, 2007). The mechanisms that have been described include:

Selective Stimulation of Beneficial Bacteria

Within the gut, prebiotics selectively stimulate endogenous bacteria such as bifidobacteria and lactobacilli, a process that leads to their fermentation into end-products such as lactic acid, acetate and butyrate (Saulnier et al, 2009).

Alteration of Short-chain Fatty Acids

Following the process of microbial transformation, prebiotics make available short-chain fatty acids (SCFAs) which are able to improve mucosal morphology by increasing mucin production (Lomax and Calder, 2008). In addition, the SCFAs so formed bind to receptors on immune cells within the GALT (Saulnier et al, 2009).

Anti-adhesive Modulation

Prebiotics can mimic binding sites by acting as a decoy for pathogen-binding cellular receptors in the gut (Saulnier et al, 2009).

Enhancement of Mineral Absorption

The absorption of minerals such as magnesium and calcium has been found to be enhanced following the administration of prebiotic agents (Saulnier et al, 2009).

Prebiotics in Specific Conditions

Alleviation of Constipation

Prebiotics have been found to exert this activity through their osmotic effects in the gut as well as their modulation of indigenous flora (Marteau and Boutron-Ruault, 2002).

Treatment of Hepatic Encephalopathy

Prebiotics such as lactulose and lactitol have demonstrated considerable superior benefits over placebos in the treatment of hepatic encephalopathy (Marteau and Boutron-Ruault, 2002). Bacterial incorporation of nitrogen as well as acidification of intestinal environment which thereby brings about reduction in the breakdown of nitrogen-containing products and other cerebral toxins have been proposed as the mechanisms used (Weber, 1996; Marteau and Boutron-Ruault, 2002).

Colon Cancer

It has been suggested that bile salts are involved in the pathogenesis of colon cancer. To this end, prebiotics have been used to decrease the faecal concentration of secondary bile salts, and the process is thought to occur via colonic pH reduction (Marteau and Boutron-Ruault, 2002).

Prebiotics and Probiotics: Constraints and Limitations

If, as observed by Thompson (2007), genetic modification of food generates a reaction of repugnance amongst many, then the concept of utilizing 'friendly' bacteria in foods certainly raise a number of stronger aesthetic objections. Such objections may even reach an 'alarming' rate if one were to consider the fact that higher levels of probiotic cells are generally thought to be necessary for a meaningful physiologic effect (Sanders, 1999; (Scrinis, 2008). Hence, suggesting the need to take increased exogenous intake of bacteria, which the lay-person has generally associated with infections and diseases.

Advocates of prebiotics and probiotics support their claim by recourse to the myriad of health benefits offered by their products, sometimes to an exaggerated extent. However, as Millar (2003) clearly points out, they often pay lip service to the various limitations of the current research method utilised in their investigations. Despite these limitations, marketers of these products in South Africa, as in elsewhere, do mislead consumers with a number of health claims that are not scientifically sound and do not conform to legislation (Brink, Senekal and Dicks, 2005).

Indeed, human studies for the evaluation of probiotic/prebiotic products have only recently begun (Saavedra and Tschernia, 2002). And while endpoints may be straightforward to define in certain cases, e.g. by measuring serum cholesterol concentrations, determining the presence or absence of immunological markers (Hamilton-Miller, 1999), only limited dose-ranging studies have been done to determine the minimum effective dose of probiotics and prebiotics. In fact, the demonstration of a reasonable level of evidence will require randomised controlled trials and consistency of results from study to study (Marteau and Boutron-Ruault, 2002)

There is actually an inherent 'temptation' offered by the use of probiotics and prebiotics, namely the tendency to create the notion in the mind of consumers that they constitute an alternative approach to the science of pharmaceutics (Afolabi et al, 2005). This is however a misguided position. We need to point out that the range of indications for which probiotics and prebiotics have been used is limited compared to those requiring pharmacologic intervention. Indeed, the repertoire of receptors expressed in the cells and tissues of the body system offer an unsurpassed choice of target sites for drugs to exert their selective therapeutic

effects. In addition, since probiotics and prebiotics generally mediate their activities via the intestinal microflora, this imposes a site-restricted limitation in relation to the possible clinical conditions in which they may be of use.

Hence, while probiotics and prebiotics have been found to be of immense health benefits, they are not to be seen as suitable drug substitutes. At best, they should be regarded as therapeutic adjuncts.

Probiotics and Prebiotics in the Nigerian Context

At this juncture, it is pertinent to mention that the idea of probiotics and prebiotics are not necessarily new to the African world. For instance, Nigerian fermented food products such as *Ogi*, *Kunnu* (pap), *Iru* (fermented locust beans), *Lafun* (fermented yam flour) and *Ogiri* (fermented melon seed) have been developed and consumed for centuries. Almost all of these have been found to contain probiotic organisms (Oyetayo and Oyetayo, 2005; Ijabaneniyi and Omoya, 2006). In fact, many of these indigenous fermented foods have been shown to exert antioxidant properties (Oboh and Amusan, 2009), a feature common to quite a number of prebiotic and probiotic food products.

From the Nigerian point of view, what is new in the contemporary application of probiotics and prebiotics is the deliberate and conscious introduction of either the so called friendly bacteria or the non-digestible oligosaccharide into the diet or a specific food product. Be that as it may, there is need to seek how the merits of this science can be gainfully appropriated. In our opinion, the vehicle of delivery of these agents would probably be the greatest factor determining how acceptable this science will be to the public. In this vein, rather than utilising such vehicle of deliveries as yoghurts, capsules and drinks (as obtained in the so-called Westernised societies), a novel approach is to make use of our local fermented foods with which almost everyone is familiar. This, we believe, will significantly dampen the extent of aesthetic rejection associated with the science of probiotics as we earlier noted.

Conclusions

In celebrating and advocating the notion of prebiotics and probiotics, a note of caution is in order. As Korthals (2005) clearly points out, food technology as well as its associated armoury (in the name of nutraceuticals, functional foods, prebiotics, probiotics, and the likes)

is neither golden nugget nor Frankenstein. That is, they inescapably suffer a number of limitations, which should always be kept in view. For instance, standardisation of daily intake of probiotics and prebiotics is often a problem (Rowland, 2004). In addition, prebiotics have the theoretical risk to increase diarrhoea in some conditions due to the osmotic effect and to be badly tolerated in patients with irritable bowel syndrome (Marteau and Boutron-Ruault, 2002).

Therefore, well-designed clinical studies in humans are still needed to further investigate the optimal dose, duration and specific effects of each probiotic strain and/or prebiotic when embedded into food matrices for specific populations such as infants and the elderly (Saulnier et al, 2009). Although much has been learned, much more remains to be learnt (Saavedra and Tschernia, 2002). In the Nigerian context, the production, standardisation and regulation of safe probiotic and prebiotic food products should be collaborative venture involving such agencies as the Federal Institute of Industrial Research (FIRO) and the National Agency for Food and Drug Administration Control (NAFDAC).

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